

Claims:

1. A probe array for qualitative and/or quantitative detection of target molecules in a sample by molecular interactions between probe molecules and target molecules on the probe array, comprising an array surface and probe molecules immobilised on the array surface at defined sites,

wherein the probe molecules have at least one label and at least one selectively cleavable bond between the site of their immobilisation on the array surface and the label.

2. The probe array of claim 1, wherein the probe molecules are selected from the group consisting of oligonucleotides, peptides, proteins and their analogues.

3. The probe array of claim 1, wherein the probe molecules are oligonucleotides.

4. The probe array of claim 3, wherein the oligonucleotides have a length of from 10 to 100 bases.

5. The probe array of claim 1, wherein the selectively cleavable bond is located approximately in the centre between the site of the immobilisation of the probe molecule on the array surface and the label.

6. The probe array of claim 1, wherein the selectively cleavable bond cannot be selectively cleaved by enzymatic methods.

7. The probe array of claim 1, wherein the selectively cleavable bond can be selectively cleaved by chemical and/or physical methods.

8. The probe array of claim 1, wherein the selectively cleavable bond can be selectively cleaved by the addition of acid anions, base cations, fluoride and/or heavy metal ions.

9. The probe array of claim 8, wherein the heavy metal ions comprise mercury ions and/or silver ions.

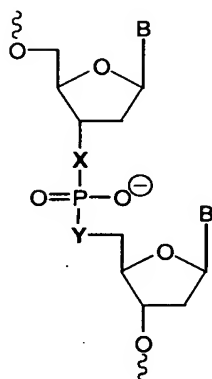
10. The probe array of claim 1, wherein the selectively cleavable bond can be selectively cleaved by photolysis.

11. The probe array of claim 1, wherein the probe molecules comprise a nucleic acid of the formula  $A_1-S-A_2$ , wherein S is a nucleic acid that comprises the at least one selectively cleavable bond, and  $A_1$  and  $A_2$  are any nucleic acids or nucleic acid analogues.

12. The probe array of claim 11, wherein S is a nucleotide dimer that is bridged by the selectively cleavable bond.

13. The probe array of claim 12, wherein S is selected from the group consisting of the following dimers having the formulae I and II:

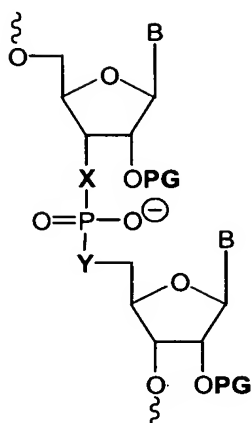
a)



I,

wherein X and Y are independently selected from the group consisting of O, NH and S, provided that X and Y are not simultaneously O; and B represents a nucleobase which is adenine, guanine, cytosine or thymine,

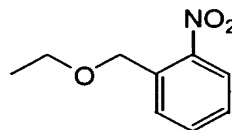
b)



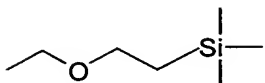
II,

wherein X and Y are independently selected from the group consisting of O, NH and S, provided that X and Y are not simultaneously O, if PG is not a labile protective group; B represents a nucleobase which is adenine, guanine, cytosine or uracil; and PG is selected from the group consisting of H

and labile protective groups such as



or



14. The probe array of claim 1, wherein the selectively cleavable bond is a phosphothioate bond.

15. The probe array of claim 1, wherein the label is a detectable unit, which is selected from the group consisting of fluorescent labels, luminescent labels, metal labels, enzyme labels, radioactive labels, polymeric labels and nucleic acids, which are detectable by hybridisation with a labelled reporter probe.

16. The probe array of claim 15, wherein the detectable unit is coupled to the probe molecules via an anchor group.

17. The probe array of claim 1, wherein the probe molecules are first probe molecules, and wherein said array further comprises second probe molecules arranged on at least

one array element of the probe array, wherein the second probe molecules have at least one label and no selectively cleavable bond.

18. The probe array of claim 17, wherein the second probe molecules are oligonucleotides having a defined or randomised sequence.

19. The probe array of claim 1, further comprising an array element having arranged thereon detectable units that are not linked to a probe molecule.

20. The probe array of claim 17, wherein the second probe molecules are arranged on different array elements which differ in their labelling degree.

21. The probe array of claim 19, wherein the detectable units are arranged on different array elements which differ in their labelling degree.

22. The probe array of claim 1, further comprising third probe molecules which have no affinity or at least no specific affinity to target molecules arranged on at least one array element.

23. The probe array of claim 22, wherein the third probe molecules are oligonucleotides with a defined or randomised sequence.

24. The probe array of claim 1, further comprising fourth probe molecules arranged on at least one array element, and which have a specific affinity to spiking target molecules which are externally added to the sample.

25. The probe array of claim 24, comprising array elements distributed over the entire surface of the array, on which said fourth probe molecules are arranged, which have a label and a selectively cleavable bond located between the label and the immobilisation site of the probe on the surface and which have a specific affinity to spiking target molecule added externally to the sample or to a target molecule present in the sample in sufficient concentration.

26. A method for producing a probe array, comprising:
- a) synthesizing probe molecules having a label and having a selectively cleavable bond between the site of their immobilisation on the array surface and the label; and
  - b) immobilizing the probe molecules via a defined position within the probe molecules at specific sites on the array surface.
27. A method for producing an array of probes on an array surface by *in situ* synthesis of the probe molecules on predetermined positions of the array surface, comprising:
- a) providing an array surface which can be activated by suitable reagents or is provided with protective groups;
  - b) coupling or immobilising subunits of the probe molecules to be synthesised to predetermined sites on the array surface; and
  - c) synthesizing the probe molecules *in situ* following said coupling or immobilizing by incorporation of a label and a selectively cleavable bond between the site of the immobilisation of the probe molecules on the array surface and the label.
28. The method of claim 27, wherein said coupling is conducted by deposition of the subunit on the array surface.
29. The method of claim 27, wherein said coupling is preceded by activation or deprotection of the array surface.
30. The method of claim 27, the probes are covalently immobilized on the array surface.
31. The method of claim 27, wherein the probes comprise oligonucleotides.
32. The method of claim 31, wherein the oligonucleotide probes are synthesized according to the phosphoramidite method.

33. The method of claim 31, wherein the selectively cleavable bond is generated by bridging two nucleosides of the probe with a phosphothioate group.

34. The method of claim 27, wherein said synthesizing the probe molecules further comprises preparing a graduated labelling degree on an array element by adding a mixture of labelled monomers and unlabelled monomers, each of the same reactivity.

35. The method of claim 34, wherein the labelled monomers and the unlabelled monomers are mixed together in a defined ratio.

36. A method of controlling the quality of a probe array for qualitative and/or quantitative detection of target molecules in a sample by molecular interactions between probe molecules and target molecules on the probe array, comprising:

- a) providing the probe array of claim 1; and
- b) detecting the probe molecules in the form of signal intensities.

37. The method of claim 36, wherein said detecting is carried out via labels to be detected directly.

38. The method of claim 37, wherein said labels are fluorescent labels or radioactive labels.

39. The method of claim 36, further comprising determining an occupation density of the array elements with probe molecules by detecting the intensity of the signals generated by the labels.

40. The method of claim 36, wherein the detection takes place by way of imaging the signal intensities in the form of degrees of greyness.

41. The method of claim 36, further comprising storing results of the quality control in a database.

42. A method for qualitative and/or quantitative detection of target molecules from a sample to be analysed by

molecular interactions between probe molecules and target molecules on probe arrays, comprising:

- a) providing the probe array of claim 1;
- b) optionally, detecting the probe molecules synthesised or immobilised on the array surface in the form of signal intensities;
- c) incubating the probe array with the sample to be analysed;
- d) optionally, washing under conditions, under which a specific interaction between the target molecules and the probe molecules remains largely stable and unspecifically bound targets are removed;
- e) optionally, detecting the probe molecules in the form of signal intensities;
- f) selectively cleaving the selectively cleavable bond in the probe molecules;
- g) optionally, washing in order to remove labelled probe molecule fragments which are not retained by an interaction with target molecules on the array surface;
- h) detecting the labelled probe molecule fragments which are retained on the array surface by an interaction with target molecules, in the form of signal intensities; and
- i) optionally, standardizing the signal intensities obtained in h).

43. The method of claim 42, wherein the standardizing in i) is carried out by at least one of the following methods:

- a) standardisation by mathematical combination of the signal intensities obtained in h) with a correction factor which is determined by the signal intensities obtained in b);
- b) standardisation of mathematical combination of the intensities obtained in h) with a correction

factor which is determined by the signal intensities of control array elements which are distributed over an entire area of the array and on which probe molecules are arranged, the probe molecules having a label and a selectively cleavable bond located between the labelling and the immobilisation site of the probe molecule on the array surface, wherein the probe molecules have a specific affinity to spiking target molecules externally added to the sample or a target molecule present in the sample in a sufficient concentration;

c) standardisation by subtraction of the signal intensities obtained in h) with the signal intensities detected of background array elements, on which probe molecules are arranged which undergo no or no detectable interaction with target molecules from the sample; and

d) standardisation by comparing the signal intensities obtained for an array element with the signal intensities of detection standard array elements, on which probe molecules are arranged, which are labelled, but not provided with a selectively cleavable bond.

44. The method of claim 42, wherein the degree of labelling of the detection standard array elements differ from the array elements in a characteristic manner.

45. The method of claim 42, wherein the selectively cleavable bond is selectively cleaved by chemical and/or physical methods.

46. The method of claim 45, wherein the selectively cleavable bond is selectively cleaved by the addition of acid anions, base cations, fluoride and/or heavy metal ions.



47. The method of claim 46, wherein the selectively cleavable bond is selectively cleaved by mercury and/or silver ions.

48. The method of claim 42, wherein the target molecules are fragmented by an enzymatic, physical or chemical method before said incubating.

49. The method of claim 42, wherein said incubating is carried out with a sample of labelled targets.

50. The method of claim 42, wherein said cleaving of the selectively cleavable bond is carried out at high ionic strength and/or low temperature.

51. A method for qualitative and/or quantitative detection of target molecules from a sample to be analysed by molecular interactions between probe molecules and target molecules on probe arrays, comprising:

- a) providing the probe array of claim 1;
- b) incubating the probe array with the sample to be analysed;
- c) selectively cleaving the selectively cleavable bond in the probe molecules; and
- d) detecting the labelled probe molecule fragments which are retained on the array surface by an interaction with target molecules, in the form of signal intensities.

52. A kit for qualitative and/or quantitative detection of target molecules from a sample by molecular interactions between probe molecules and target molecules on probe arrays, comprising:

- a) the probe array of claim 1;
- b) reagents for the selective cleavage of the selectively cleavable bond in the probe molecules;
- c) hybridisation buffer; and
- d) optionally, washing buffer.

53. The kit of claim 52, wherein the reagents are selected from the group consisting of heavy metal ions and enzymes.

54. The kit of claim 53, wherein the heavy metal ions are selected from mercury ions and/or silver ions.

55. The kit of claim 52, further comprising a reaction chamber.

56. The kit of claim 52, further comprising a detection device.

57. The kit of claim 52, further comprising a temperature control unit.

58. The kit of claim 52, wherein the probe array is in the form of a highly integrated autonomous unit.

59. A method for the production of monomer building blocks suitable for DNA synthesis, which can be used for the formation of a labile bond in probe molecules, comprising:

- a) esterifying the 5'-OH group of a nucleoside with an acid suitable as leaving group, to produce an ester;
- b) reacting the ester with a thioester;
- c) saponifying the thioester to form a thiol;
- d) protecting the thiol function with protective groups suitable for the phosphotriester or phosphoramidite method; and
- e) activating the protected thiol at the 3' position using the phosphotriester or phosphoramidite method.

60. A method for the production of monomer building blocks suitable for DNA synthesis, which can be used for the formation of a labile bond in probe molecules, comprising:

- a) reacting a compound suitable as a protective group for the phosphotriester or phosphoramidite method to form a thiol;

- b) esterifying the 5'-OH group of a nucleoside with an acid suitable as leaving group, to form an ester;
- c) reacting the thiol of a) with the ester of b); and
- d) activating the protected thiol at the 3' position using the phosphotriester or phosphoramidite method.

61. The compound 5'-S-(dimethoxytrityl)-mercapto-5'-deoxynucleoside-3'-O-(2-cyanoethyl, N,N'-diisopropylphosphite).